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WILMERHALE/BOSTON
60 STATE STREET
BOSTON, MA 02109

EXAMINER	
GANGLE, BRIAN J	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

michael.mathewson@wilmerhale.com
teresa.carvalho@wilmerhale.com
sharon.matthews@wilmerhale.com

Office Action Summary	Application No.	Applicant(s)	
	09/890,335	CEVC ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37,38,40-43,45-66 and 68-79* is/are pending in the application.

4a) Of the above claim(s) *46,49,51-54,56,57,61 and 68-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-38, 40-43, 45, 47-48, 50, 55, 58-60, and 62-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and remarks, filed on 11/3/2008, are acknowledged. Claims 37-38, 40-43, 45, 47-48, 50, 55, 58-60, and 62-66 are amended. Claim 44 is cancelled. Claims 37-38, 40-43, 45-66, and 68-79 are pending. Claims 46, 49, 51-54, 56-57, 61, and 68-79 are withdrawn as being drawn to non-elected inventions. Claims 37-38, 40-43, 45, 47-48, 50, 55, 58-60, and 62-66 are currently under examination.

New Objections

Claim 64 is objected to because of the following informalities: the claim refers to the units "mg/cm2." This should read mg/cm^2. Appropriate correction is required.

Claim Rejections Withdrawn

The rejection of claims 38-45, 47-48, 50, 55, 58-60, and 62-66 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for vaccines comprising tetanus toxoid as the antigen, does not reasonably provide enablement for vaccines comprising an antigen derived from pathogens triggering tetanus, is withdrawn in light of applicant's amendment thereto.

The rejection of claims 38, 40-45, 47-48, 50, 55, 58-60, and 62-67 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in light of applicant's amendment thereto.

Claim Rejections Maintained

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 37 and amended claims 38, 40-41, 58-59, and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Paul *et al.* (Vaccine Res., 4:145-164, 1995, IDS filed 12/30/2003), for the reasons set forth in the previous office action in the rejection of claim 37.

The instant claim is drawn to a transdermal antigenic composition, comprising: (a) a transdermal carrier comprising a penetrant suspended or dispersed in an aqueous solvent, the penetrant in the form of a minute fluid droplet surrounded by a coating of one or more layers of at least 2 substances that differ by at least a factor of 10 in solubility, the substances forming homoaggregates of one substance and/or heteroaggregates of the at least 2 substances, the average diameter of homoaggregates of the more soluble substance, or the average diameter of the heteroaggregates of the at least 2 substances, being smaller than the average diameter of homoaggregates of the less soluble substance, and/or the more soluble substance solubilizing the droplet and the content of the more soluble substance being up to 99 mol-% of the concentration required to solubilize the droplet or corresponding to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or wherein the elastic deformation energy of the droplet surrounded by the coating is at least 5 times lower than the elastic deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains; (b) a compound which specifically has or induces cytokine or anti- cytokine activity; (c) an antigen or mixture thereof and/or an allergen or mixture thereof; and (d) a chemical irritant.

Paul *et al.* disclose a transdermal carrier (see page 146, paragraph 3) known as a transfersome that comprises ethanolic soybean phosphatidylcholine, sodium cholate, an antigen (purified BSA), and a compound which induces cytokine activity (lipid A) (see page 148, Transfersomes preparation). Sodium cholate is a surfactant and therefore an irritant. Additionally, the composition contains triethanolamine, which is an irritant (see page 148, Transfersomes preparation). Regarding claim 38, the transfersomes of Paul include sodium cholate, which is the conjugate base of cholic acid. In all acid-base reactions, the acid will react with a base to form the conjugate base and vice versa, switching ionization states. The dissociation constant of sodium cholate is such that, in the transfersome composition of Paul, there would be two ionization states of sodium cholate. Regarding claim 40, phosphatidylcholine is a polar lipid and sodium cholate is a surfactant. Said transfersomes have

the same composition as the claimed vaccine carrier and would thus necessarily have the same physical and immunological properties as the claimed vaccine transfersomes.

Applicant argues:

1. That the composition of Paul does not include a chemical irritant and/or an extract of a compound from a pathogen, a fragment or a derivative of the chemical irritant, or compound isolated from a pathogen.

Applicant's arguments have been fully considered and deemed non-persuasive.

As discussed above, the composition of Paul contains sodium cholate, which is a surfactant and therefore an irritant. The composition also contains triethanolamine which is an irritant.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 37-38, 40-45, 47-48, 50, 55, 58-60, and 62-66 under 35 U.S.C. 103(a) as being unpatentable over Glenn *et al.* (PCT Publication, WO 98/20734, 1998) in view of Paul *et al.* (Vaccine Res., 4:145-164, 1995, IDS filed 12/30/2003), is maintained for the

reasons set forth in the rejection of claims 37, 39-45, 47-48, 50, 55, 58-60, and 62-67 in the previous office action.

Applicant argues:

1. Applicant disagrees with the examiner's contentions, set forth in the previous office action, regarding unexpected results. Applicant argues that they have not misstated the MPEP and refers to MPEP 716.02(a)(I), which is entitled, "Greater Than Expected Results Are Evidence of Nonobviousness." Applicant also refers to the MPEP citation of *In re Corkill* and states that the MPEP states that "a particular unexpected result 'was persuasive of nonobviousness.'"

2. That the case law cited in the office action does not stand for the naked principle that unexpected results do not overcome a strong case of obviousness.

3. That, none of the cited case law disproves the premise that while it is true that unexpected results must be weighed with all the evidence, if unexpected results are commensurate with the claims and are indeed unexpected in view of what was taught in the art, such results would almost certainly establish that the claims were not obvious.

Applicant asserts that the *Anderson's* court found a conclusion that a design was not obvious was supported by evidence showing the elements of the design worked together in an unexpected and fruitful manner.

Applicant asserts that *In re Oetiker* did not rule on this point at all.

Applicant asserts that that *In re Chupp* stands for the principle that a compound need not excel over prior art compounds in all common properties.

Applicant asserts that *Newell* does not stand for the proposition that a strong showing of obviousness should be maintained in the face of a showing of unexpected properties that are commensurate in scope with the claims.

Applicant asserts that *Richardson-Vick's* also provides no support of the examiner's position. Applicant asserts that in that case, the court discounted the showing of unexpected results not because such results can be overcome by a strong showing of obviousness, but because the alleged property was unknown at the time of invention.

Applicant also states that in their previous arguments, applicant was not stating or even suggesting that a weighing of the evidence was not necessary.

4. That the claimed compositions have yielded unexpected properties over what the cited art teaches was expected. To support this, applicant refers to Paul, which states, "immunoadjuvants do not necessarily strengthen the immune response when using transdermal immunization." Applicant argues that Paul explicitly sets forth that co-stimulatory factors did not improve the immune response and were unnecessary to produce an improved protected immune response. Applicant argues that they have unexpectedly shown that co-stimulatory factors induce an improved immune response.

5. That Glenn and Paul teach away from one another. Applicant argues that Glenn specifically sets itself apart from Paul and touts the advantages of it's particular transdermal delivery system. Applicant states that Glenn refers to Paul and states that "formulations of antigen in solution, antigen and mixed micelles, and antigen and liposomes... applied to the skin did not induce an immune response equivalent to that induced subcutaneous injection." Applicant argues that Glenn was actively trying to develop formulations that would not require the transfersomes of the instant invention and one of skill in the art would not combine these disclosures to achieve the instant invention.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, applicant has cited MPEP 716.02(a), *KSR International Co. v. Teleflex Inc.*, No. 04-1350 (U.S. Apr. 30, 2007), and *In re Corkill,* 711 F.2d 1496, (Fed. Cir. 1985), stating that "even if references and/or the knowledge of those of skill in the art teach or suggest all of the limitations of a claim, an obviousness rejection is overcome by a showing of unexpected results" and "evidence showing a greater than expected result is persuasive of nonovbiousness." This is not what the MPEP or the cited case law states or even implies. The title referred to by applicant is "Greater Than Expected Results Are Evidence of Nonobviousness." Evidence of nonobviousness is not the same as persuasive of nonobviousness. Neither *KSR* nor *Corkill* state what applicant are arguing. *Corkill* states, "a greater than expected result is an evidentiary factor pertinent to the legal conclusion of obviousness." This does not mean that evidence of secondary considerations *is* persuasive of obviousness, as applicant suggests.

Regarding argument 2, applicant is absolutely correct. Likewise, the case law cited in the MPEP and by applicant do not stand for the naked principle that unexpected results do overcome

a strong case of obviousness. As stated previously, the existence of such evidence, does not control the obviousness determination. Paul provides an explicit suggestion that an adjuvant be included in the composition, stating "immunoadjuvants thus improve the reproducibility of the transdermal immunization significantly and also minimize the antigen dose effects" (page 155, paragraph 3).

Regarding argument 3, applicant states that they were not suggesting that a weighing of the evidence is not necessary. However, applicant stated previously, and again in this action, that "even if references and/or the knowledge of those of skill in the art teach or suggest all of the limitations of a claim, an obviousness rejection is overcome by a showing of unexpected results" and "evidence showing a greater than expected result is persuasive of nonovbiousness." These statements clearly imply that no weighing of evidence is necessary and that evidence of unexpected results is automatically persuasive of nonobviousness.

Even if applicant's assertions are correct, the "showing of unexpected results" in this case is not commensurate in scope with the claims. The instant claims are drawn to *any* co-stimulatory molecule. This includes the lipid A and muramyl dipeptide used in the Paul reference. These are the same co-stimulatory molecules that applicant has argued are not effective in increasing the immune response.

Applicant's assertions regarding the case law are also not correct. The *Anderson* court did not find that a design was not obvious because the elements worked together in an unexpected and fruitful manner. In fact, the *Anderson* court found that the combination *was* obvious because the two old elements did nothing more in combination than they did separately.

In re Oetiker states "patentability is determined on totality of record, by preponderance of evidence with due consideration to persuasiveness of argument," which is precisely the point the examiner was making.

While applicant does accurately state the findings of the court in *In re Chubb*, the case also states, "mere submission of some evidence that a new compound possesses some unpredictable properties does not require an automatic conclusion of nonobviousness in every case," which is again, the point the examiner has made.

Newell reiterates this point. *Newell* shows that a strong case of obviousness can overcome evidence of secondary considerations, stating, "secondary factors must be considered but do not control obviousness determination."

Applicant's summary of *Richardson-Vick's* is again incorrect. In fact, the court found that "unexpected results and commercial success of claimed invention, although supported by substantial evidence, do not overcome clear and convincing evidence of obviousness." *Richardson-Vick's* is actually the case most related to the instant case. While there was a great deal of evidence of both unexpected results and commercial success, there was a very clear indication that the invention was obvious. This is similar to the instant invention in that, regardless of the "unexpected results" purported by applicant, the Paul reference specifically suggests the use of co-stimulatory factors. There could be no clearer an indication that a co-stimulator factor should be used.

The sum total of the case law and the direction of the MPEP is clear: Evidence of secondary considerations, including evidence of unexpected results and commercial success, are but a part of the "totality of the evidence" that is used to reach the ultimate conclusion of obviousness. *Kansas Jack* , 719 F.2d at 1151, 219 USPQ at 862. In some cases such evidence is the most probative of obviousness. *See, e.g.* , *Stratoflex* , 713 F.2d at 1538, 218 USPQ at 879. The existence of such evidence, however, does not control the obviousness determination. *See Newell* , 864 F.2d at 768, 9 USPQ2d at 1426 ("First, as indicated, obviousness is not a factual inference; second, although these factors must be considered, they do not control the obviousness conclusion.") (citations omitted); *Ryko* , 950 F.2d at 719, 21 USPQ2d at 1058 (the weight of secondary considerations may be of insufficient weight to override a determination of obviousness based on primary considerations).

Regarding argument 4, the "showing of unexpected results" in this case is not commensurate in scope with the claims. The instant claims are drawn to *any* co-stimulatory molecule. This includes the lipid A and muramyl dipeptide used in the Paul reference. These are the same co-stimulatory molecules that applicant argues are not effective in increasing the immune response. It is important to note that Paul states that "immunoadjuvants do not necessarily strengthen the immune response when using transdermal immunization." The important words in this statement are "do not necessarily." Paul only tested two adjuvants.

These did not strengthen the immune response but this does not provide any teaching whatsoever regarding other immunoadjuvants. The more important fact that applicant is ignoring is that Paul specifically provides a reason for including immunoadjuvants, stating "immunoadjuvants thus improve the reproducibility of the transdermal immunization significantly and also minimize the antigen dose effects" (page 155, paragraph 3). Paul also states "the effect of adjuvants is relatively more important for the sparsely dosed immunogens" (page 154, paragraph 4). Thus, Paul provides a strong suggestion that an adjuvant should be included in their composition. While a given adjuvant might not strengthen the immune response, it does serve other purposes. The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Where the prior art provides other motivation to select a particular species or subgenus, a showing of a new use may not be sufficient to confer patentability. See *Dillon*, 919 F.2d at 692, 16 USPQ2d at 1900-01. Finally, see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 (U.S. Apr. 30, 2007), "the problem motivating the patentee may be only one of many addressed by the patent's subject matter. The question is not whether the combination was obvious to the patentee but whether the combination was obvious to a person with ordinary skill n the art. Under the correct analysis, any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed."

Regarding argument 5, the fact Glenn differentiates itself from Paul is neither surprising nor relevant. Obviously, one would expect Glenn to differentiate himself from Paul and to praise his own invention. However, the nature of the teachings is important. Glenn was not cited to show a transdermal composition. Paul teaches transfersomes as an effective transdermal immunization means. Paul lacks the inclusion of tetanus toxoid and IL-12 in the transfersomes. Glenn teaches a transdermal vaccine containing tetanus toxoid and IL-12. Any number of references could have been cited to teach IL-12 as an adjuvant and tetanus toxoid as a vaccine antigen; these are well known. Glenn was chosen because it suggests transdermal delivery of these.

With regard to the cited portion of Glenn, the quote refers to liposomes, micelles, and antigens in solution, making no mention whatsoever of transfersomes. Thus, the quote is not relevant.

The fact that the references describe different and incompatible transdermal delivery systems does not prevent a combination of the references. The examiner is not suggesting that the inventions of Glenn and Paul could be literally combined. The antigen and adjuvant of Glenn could be used in the transfersomes of Paul. There is no incompatibility between the references that would prevent such a combination. Furthermore, the fact that Glenn had a successful system does not teach away from a combination with Paul. MPEP 2123 states that disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi,* 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994).

As outlined previously, the instant claims are drawn to a transdermal antigenic composition, comprising: (a) a transdermal carrier comprising a penetrant suspended or dispersed in an aqueous solvent, the penetrant in the form of a minute fluid droplet surrounded by a coating of one or more layers of at least 2 substances that differ by at least a factor of 10 in solubility, the substances forming homoaggregates of one substance and/or heteroaggregates of the at least 2 substances, the average diameter of homoaggregates of the more soluble substance, or the average diameter of the heteroaggregates of the at least 2 substances, being smaller than the average diameter of homoaggregates of the less soluble substance, and/or the more soluble substance solubilizing the droplet and the content of the more soluble substance being up to 99 mol-% of the concentration required to solubilize the droplet or corresponding to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or wherein the elastic deformation energy of the droplet surrounded by the coating is at least 5 times lower than the elastic deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains; (b) a compound which specifically has or induces cytokine or anti- cytokine activity; (c) an antigen or mixture thereof and/or an allergen or mixture thereof; (d) comprising a chemical irritant and/or an extract or compound from a pathogen or a fragment or a derivative of

the irritant, pathogen compound, or extract. Further limitations include: the antigenic composition of claim 37 wherein the at least two substances are two ionization states or salt forms of the same substance (claim 38); the antigenic composition wherein the less soluble substance with the tendency to aggregate is a polar lipid, and the more soluble substance is a surfactant (claim 40); wherein the penetrant is between 30 nm and 500 nm (claim 41); wherein the total weight of droplets in the antigenic composition for use on human or animal skin is 0.01 weight-% to 40 w-% of total mass (claim 42); wherein total antigen concentration is between 0.001 and 40 w-% of the total penetrant mass (claim 43); wherein the compound is IL-12 (claim 45); wherein the antigen is derived from *Clostridium tetani* (claims 47-48); wherein the concentration of each compound used is up to 1000 times higher than a concentration optimum established in corresponding tests performed by injecting the antigenic composition or performing the tests *in vitro* (claim 50); wherein the concentration of the compound from a pathogen is between 10 times lower and up to 1000 times higher than the concentration used with the corresponding injected the antigenic composition employing similar antigen (claim 55); wherein the irritant is selected from the group consisting of surfactants and derivatives and combinations thereof (claim 58); wherein the surfactant enhances skin permeation (claim 59); wherein the concentration of the irritant is below by at least a factor of 2 to a factor of 10 or more a concentration which is unacceptable owing to local irritation in tests on the same or a comparable subject (claim 60); wherein the applied dose of the antigen differs by the factor of 0.1 to 100 from the dose which would have to be used with an injection (claim 62); wherein the applied dose of an antigen is less than 10 times higher than the dose which would have to be used with an injection (claim 63); wherein the applied penetrant dose is between 0.1 mg/cm^2 and 15 mg/cm^2 (claim 64); and wherein the antigen is a pure of purified antigen (claim 65). Further claims are drawn to a kit containing the vaccine of claim 37 in a packaged form (claim 66).

Glenn *et al.* disclose a transdermal vaccine that contains tetanus toxoid and interleukin-12 (see abstract; page 16, lines 15-17; and page 18, lines 15-30). Glenn *et al.* state that the antigens used in the vaccine can be purified (see paragraph bridging pages 15-16).

Glenn *et al.* differs from the instant invention in that the transdermal vaccine does not comprise a carrier wherein the substances forming homoaggregates of one substance and/or heteroaggregates of the at least 2 substances, the average diameter of homoaggregates of the

more soluble substance, or the average diameter of the heteroaggregates of the at least 2 substances, being smaller than the average diameter of homoaggregates of the less soluble substance, and/or the more soluble substance solubilizing the droplet and the content of the more soluble substance being up to 99 mol-% of the concentration required to solubilize the droplet or corresponding to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or wherein the elastic deformation energy of the droplet surrounded by the coating is at least 5 times lower than the elastic deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains.

Paul *et al.* disclose an transdermal vaccine (see page 146, paragraph 3) that comprises a transdermal carrier known as a transfersome that comprises ethanolic soybean phosphatidylcholine, sodium cholate, and an antigen (see page 148, Transfersomes preparation). Said transfersomes have the same composition as the claimed vaccine carrier and would thus necessarily have the same physical and immunological properties as the claimed vaccine transfersomes. Additionally, Paul *et al.* disclose that transdermal immunization using large protein molecules can be accomplished using said transfersomes, and that, if properly optimized, a transdermal drug transfer efficacy of > 90% can be achieved (see page 162, paragraphs 7-8). Paul *et al.* further disclose that vaccination can be accomplished using full size proteins across the intact skin (see page 146, paragraph 3).

It would have been obvious to one of ordinary skill in the art to use the transdermal carrier (transfersomes) of Paul *et al.* in the vaccine of Glenn *et al.* in order to take advantage of the high drug transfer efficacy of transfersomes, as disclosed by Paul *et al.* One would have had a reasonable expectation of success because Paul *et al.* disclose that their transfersomes are capable of delivering full size proteins across the skin in a vaccination. Regarding claim 38, the transfersomes of Paul include sodium cholate, which is the conjugate base of cholic acid. In all acid-base reactions, the acid will react with a base to form the conjugate base and vice versa, switching ionization states. The dissociation constant of sodium cholate is such that, in the transfersome composition of Paul, there would be two ionization states of sodium cholate. Regarding claim 40, phosphatidylcholine is a polar lipid and sodium cholate is a surfactant. Regarding claims 44 and 58, sodium cholate is a surfactant and therefore and irritant. Regarding claims 41-43, 50, 55, 60, and 62-64, these claims are merely optimized ranges for materials in

the vaccine. Paul *et al.* disclose that the vaccine should be properly optimized to achieve efficacy. Further, according to MPEP 2144.05, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Regarding claim 66, the vaccine disclosed by the prior art are packaged in some form, thus anticipating the limitation of a kit containing said vaccine in a packaged form. Therefore, as the vaccine disclosed by the prior art contains a dose of antigen, the prior art anticipates this limitation.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571)272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brian J Gangle/
Examiner, Art Unit 1645
/Mark Navarro/
Primary Examiner, Art Unit 1645